

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)



REC'D 28 FEB 2005

WIPO PCT

Applicant's or agent's file reference 33152PC01	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/DK 03/00788	International filing date (day/month/year) 18.11.2003	Priority date (day/month/year) 18.11.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/7088		
Applicant SANTARIS PHARMA AS et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 12 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☒ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 08.06.2004	Date of completion of this report 24.02.2005
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Beeck, M Telephone No. +49 89 2399-8473 

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I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-42 as originally filed

Claims, Numbers

1-42 as originally filed

Drawings, Sheets

1/23-23/23 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

- ☐ restricted the claims.
☐ paid additional fees.
☐ paid additional fees under protest.
☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
☒ not complied with for the following reasons:

see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-42
Inventive step (IS)	Yes: Claims	
	No: Claims	1-42
Industrial applicability (IA)	Yes: Claims	1-42
	No: Claims	

2. Citations and explanations

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see separate sheet

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- D1: KUMAR RAVINDRA ET AL: "The first analogues of LNA (locked nucleic acids): Phosphorothioate-LNA and 2'thio-LNA" BIOORGANIC AND MEDICINAL CHEMISTRY LETTERS, vol. 8, no. 16, 18 August 1998 (1998-08-18), pages 2219-2222, XP002281372 ISSN: 0960-894X
- D2: SINGH S K ET AL: "SYNTHESIS OF 2'-AMINO-LNA: A NOVEL CONFORMATIONALLY RESTRICTED HIGH-AFFINITY OLIGONULEOTIDE ANALOGUE WITH A HANDLE" JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY. EASTON, US, vol. 63, no. 26, 1998, pages 10035-10039, XP002901079 ISSN: 0022-3263
- D3: WO 01/48190 A (EXIQON AS ;KOCH TROELS (DK); ORUM HENRIK (DK); SKOUV JAN (DK); JAK) 5 July 2001 (2001-07-05)
- D4: SORENSEN MADSD ET AL: "alpha-L-ribo-configured locked nucleic acid (alpha-L-LNA): Synthesis and properties" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 124, no. 10, 13 March 2002 (2002-03-13), pages 2164-2176, XP002281373 ISSN: 0002-7863
- D5: KEINICKE LISE ET AL: "alpha-L-RNA (alpha-L-ribo configured RNA): Synthesis and RNA-selective hybridization of alpha-L-RNA/alpha-L-LNA chimera" BIOORGANIC AND MEDICINAL CHEMISTRY LETTERS, vol. 12, no. 4, 25 February 2002 (2002-02-25), pages 593-596, XP002281374 ISSN: 0960-894X
- D6: WO 00/66604 A (EXIQON AS ;WENGEL JESPER (DK)) 9 November 2000 (2000-11-09)
- D7: WO 01/25478 A (EXIQON AS ;KOSHKIN ALEXEI (DK); JAKOBSEN MOGENS HAVSTEEN (DK)) 12 April 2001 (2001-04-12)
- D8: KURRECK JENS ET AL: "Design of antisense oligonucleotides stabilized by locked nucleic acids" NUCLEIC ACIDS RESEARCH, vol. 30, no. 9, 1 May 2002 (2002-05-01), pages 1911-1918, XP002281375 ISSN: 0305-1048
- D9: WO 01/25248 A (EXIQON AS ;JAKOBSEN MOGENS HAVSTEEN (DK); WAHLESTEDT CLAES (SE)) 12 April 2001 (2001-04-12)
- D10: FRIEDEN MIRIAM ET AL: "Expanding the design horizon of antisense oligonucleotides with alpha-L-LNA." NUCLEIC ACIDS RESEARCH, vol. 31, no. 21, 1 November 2003 (2003-11-01), pages 6365-6372, XP002281376 ISSN: 0305-1048 (ISSN print)

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SECTION IV:

This Authority considers that there are two inventions covered by the claims indicated as follows:

I: Claims 1-31 and 32 to 38 as far as they are directed to amino-LNA, thio-LNA or α -

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II: Claims 32 to 38 directed to oligonucleotide constructs of the formula A-B-C-D (A,

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The reason for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, is that the chemical structures of the compounds of the two inventions are not interrelated.

SECTION V:

- 1) The examination has been carried out assuming that the priority is valid, so that P-document D10 has not been taken into consideration.
- 2) An oligonucleotide construct as claimed in present claim 10 is already known from documents D1 (see the table on page 2221), D2 (see table 1 on page 10037), D3 (see example 1), D4 (see figure 3), D5 (see table 1) and D6 (see example 10 and table 3).

Therefore the subject-matter of claims 10 to 31 and 39 to 42 is not novel (Article 33 (2) PCT).

- 2) Pharmaceutical compositions of such oligonucleotide constructs are also known, namely from document D3 (see example 1).

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This document also anticipates the subject-matter of claims 1 to 9 so that these claims are not novel either.

- 3) Documents D7 (see tables 1 to 4), D8 (see table 1) and D9 (see the example) already disclose oligonucleotides falling under the formulae of claims 32 to 38, so that these claims are not novel either.